

WHAT IS CLAIMED IS:

1. A luminal prosthesis comprising:
a scaffold which is implantable within a body lumen; and
means on the scaffold for releasing a substance, wherein the substance is released over a predetermined time pattern comprising an initial phase wherein a substance delivery rate is below a threshold level and a subsequent phase wherein the substance delivery rate is above a threshold level.
2. A luminal prosthesis as in claim 1, wherein the scaffold is a stent or graft.
3. A luminal prosthesis as in claim 1, wherein the scaffold is implantable in a blood vessel.
4. A luminal prosthesis as in claim 1, wherein the substance comprises at least one agent selected from the group consisting of immunosuppressant agent, anti-inflammatory agent, anti-proliferative agent, anti-migratory agent, anti-fibrotic agent, anti-thrombotic agent, anti-platelet agent, and IIb/IIIa agent.
5. A luminal prosthesis as in claim 4, wherein the agent is at least one immunosuppressant agent selected from the group consisting of mycophenolic acid, rapamycin, cyclosporine A, cycloheximide, cyclophosphamide, mizoribine, methylprednisolone, azathioprine, ribovirin, FK506, tiazofurin, methotrexate, zafurin, and mycophenolate mofetil.
6. A luminal prosthesis as in claim 1, wherein the means for releasing the substance comprises a matrix formed over at least a portion of the scaffold.
7. A luminal prosthesis as in claim 6, wherein the matrix is composed of a material which undergoes degradation in a vascular environment.
8. A luminal prosthesis as in claim 7, wherein the matrix degrades by surface degradation.
9. A luminal prosthesis as in claim 7, wherein the matrix degrades by bulk degradation.

- 1 10. A luminal prosthesis as in claim 7, wherein the matrix is a copolymer
2 of poly-l-lactic acid and poly-e-caprolactone.
- 1 11. A luminal prosthesis as in claim 6, wherein the matrix is composed of
2 a nondegradable material.
- 1 12. A luminal prosthesis as in claim 11, wherein the nondegradable matrix
2 comprises cellulose acetate butyrate.
- 1 13. A luminal prosthesis as in claim 6, wherein the substance is disposed
2 within the matrix in a pattern that provides the desired release rates.
- 1 14. A luminal prosthesis as in claim 6, wherein the substance is on or
2 within the scaffold adjacent the matrix in a pattern that provides the desired release rates.
- 1 15. A luminal prosthesis as in claim 6, wherein the matrix comprises
2 multiple layers, each layer containing a different, same, or no substance.
- 1 16. A luminal prosthesis as in claim 6, further comprising a rate limiting
2 barrier coupled to the matrix.
- 1 17. A luminal prosthesis as in claim 6, further comprising a rate limiting
2 barrier formed over the matrix.
- 1 18. A luminal prosthesis as in claim 16 or 17, wherein the substance is
2 released by diffusion through the barrier.
- 1 19. A luminal prosthesis as in claim 6, further comprising a biocompatible
2 layer coupled to the matrix.
- 1 20. A luminal prosthesis as in claim 1; wherein the means for releasing the
2 substance comprises a rate limiting barrier formed over at least a portion of the scaffold.
- 1 21. A luminal prosthesis as in claim 20, wherein the rate limiting barrier
2 has a sufficient thickness so that release of the substance from the barrier begins substantially
3 after a preselected time period.

1 22. A luminal prosthesis as in claim 20, wherein the barrier has a thickness
2 in a range from 0.01 micron to 100 microns.

1 23. A luminal prosthesis as in claim 20, wherein the barrier is composed of
2 at least one material selected from the group consisting of silicone, polytetrafluoroethylene,
3 parylast, polyurethane, and paralene.

1 24. A luminal prosthesis as in claim 20, wherein the barrier comprises
2 multiple layers, each layer containing a different, same, or no substance.

1 25. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and a
3 cover over the reservoir, wherein the cover is at least partially degradable over a preselected
4 time period so that release of the substance from the reservoir begins substantially after the
5 preselected time period.

6 26. A luminal prosthesis as in claim 25, wherein the cover is a polymer
7 matrix.

8 27. A luminal prosthesis as in claim 25, further comprising a rate limiting
9 barrier formed between the reservoir and the cover.

10 28. A luminal prosthesis as in claim 25, further comprising a rate limiting
11 barrier coupled to the cover.

1 29. A luminal prosthesis as in claim 27 or 28, wherein the substance is
2 released by diffusion through the barrier.

1 30. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and a
3 cover over the reservoir.

1 31. A luminal prosthesis as in claim 30, wherein the cover having a
2 sufficient thickness so that release of the substance from the reservoir begins substantially
3 after a preselected time period.

1 32. A luminal prosthesis as in claim 30, wherein the cover is a
2 nondegradable matrix.

1 33. A luminal prosthesis as in claim 30, wherein the cover is a rate limiting
2 barrier.

1 34. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and an
3 external energy source for directing energy at the prosthesis after implantation to effect
4 release of the substance.

1 35. A luminal prosthesis as in claim 34, further comprising a matrix over
2 the reservoir.

1 36. A luminal prosthesis as in claim 34, further comprising a rate limiting
2 barrier over the reservoir.

1 37. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a matrix formed over at least a portion of the scaffold, wherein the
3 substance is disposed adjacent or within the matrix, and an external energy source for
4 directing energy at the prosthesis after implantation to effect release of the substance.

1 38. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a rate limiting barrier formed over at least a portion of the scaffold,
3 wherein the substance is disposed adjacent or within the barrier, and an external energy
4 source for directing energy at the prosthesis after implantation to effect release of the
5 substance.

1 39. A luminal prosthesis as in any of claims 34, 37, or 38, wherein the
2 energy source is at least one of ultrasound, magnetic resonance imaging, magnetic field, radio
3 frequency, temperature change, electromagnetic, x-ray, radiation, heat, gamma, or
4 microwave.

1 40. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to the substance or the scaffold and a

3 magnetic source for directing a magnetic field at the prosthesis after implantation to effect
4 release of the substance.

1 41. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to a matrix formed over the scaffold and a
3 magnetic source for directing a magnetic field at the prosthesis after implantation to effect
4 release of the substance.

1 42. A luminal prosthesis as in claim 41, wherein the substance is disposed
2 adjacent or within the matrix.

1 43. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to a rate limiting barrier formed over the
3 scaffold and a magnetic source for directing a magnetic field at the prosthesis after
4 implantation to effect release of the substance.

1 44. A luminal prosthesis as in claim 43, wherein the substance is disposed
2 adjacent or within the barrier.

1 45. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a change in a pH to effect release of the substance.

1 46. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and
3 vibrational or heating energy directed at the prosthesis after implantation to effect release of
4 the substance.

1 47. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises at least a matrix or rate limiting barrier formed over the scaffold
3 containing the substance and vibrational or heating energy directed at the prosthesis after
4 implantation to effect release of the substance.

1 48. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is less than 12 weeks.

1 49. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 1 hour to 8 weeks.

- 1 50. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 12 hours to 2 weeks.
- 1 51. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 1 day to 1 week.
- 1 52. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 4 hours to 24 weeks.
- 1 53. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 1 day to 12 weeks.
- 1 54. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 2 days to 8 weeks.
- 1 55. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 3 days to 50 days.
- 1 56. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the initial phase is between 0 $\mu\text{g/day}$ to 50 $\mu\text{g/day}$.
- 1 57. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the initial phase is between 5 $\mu\text{g/day}$ to 30 $\mu\text{g/day}$.
- 1 58. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the subsequent phase is between 5 $\mu\text{g/day}$ to 200 $\mu\text{g/day}$.
- 1 59. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the subsequent phase is between 10 $\mu\text{g/day}$ to 100 $\mu\text{g/day}$.
- 1 60. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the initial phase is within a range from 0 $\mu\text{g/mg}$ of tissue to
3 100 $\mu\text{g/mg}$ of tissue.
- 1 61. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the initial phase is within a range from 0 $\mu\text{g/mg}$ of tissue to
3 10 $\mu\text{g/mg}$ of tissue.

62. A luminal prosthesis as in claim 1, wherein a mammalian tissue concentration of the substance at the subsequent phase is within a range from 1 picogram/mg of tissue to 100 µg/mg of tissue.

63. A luminal prosthesis as in claim 1, wherein a mammalian tissue concentration of the substance at the subsequent phase is within a range from 1 nanogram/mg of tissue to 10 µg/mg of tissue.

64. An improved method for delivering a pharmacological agent to an artery, said method being of the type where a prosthesis is implanted within the artery and the prosthesis releases the pharmacological agent, wherein the improvement comprises implanting a prosthesis that is programmed to begin substantial release of the pharmacological agent beginning after growth of at least one layer of cells over a part of the prosthesis.

65. A method as in claim 64, wherein the cells comprise inflammatory, smooth muscle, or endothelial cells.

66. A method as in claim 64, wherein the pharmacological agent comprises at least one agent selected from the consisting of immunosuppressant agent, anti-inflammatory agent, anti-proliferative agent, anti-migratory agent, anti-fibrotic agent, anti-thrombotic agent, anti-platelet agent, and IIb/IIIa agent.

67. A method for luminal substance delivery, said method comprising: providing a luminal prosthesis incorporating or coupled to the substance, wherein the prosthesis contains a matrix which undergoes degradation in a vascular environment; and

implanting the prosthesis in a body lumen so that at least a portion of the matrix degrades over a predetermined time period and substantial substance release begins after the matrix substantially begins to degrade.

68. A method as in claim 67, wherein the substance is incorporated in a reservoir in or on a scaffold and the reservoir is covered by the matrix so that substantial substance release begins after the matrix has degraded sufficiently to uncover the reservoir.

1 69. A method as in claim 67, wherein the substance is contained in the
2 matrix and the matrix coats a scaffold, wherein an outer layer of the matrix is substantially
3 free from the substance so that substance release will not substantially begin until the outer
4 layer has degraded.

1 70. A method as in claim 67, wherein the substance is contained within or
2 on a scaffold coated by the matrix.

1 71. A method as in claim 67, wherein the prosthesis is coated with the
2 matrix by spraying, dipping, deposition, or painting.

1 72. A method as in claim 67, wherein the prosthesis incorporates the
2 substance by coating, spraying, dipping, deposition, or painting the substance on the
3 prosthesis.

73. A method as in claim 67, wherein the matrix is a polymer.

1 74. A method as in claim 67, wherein the matrix comprises multiple
2 layers, each layer containing a different, same, or no substance.

1 75. A method as in claim 67, wherein the prosthesis contains a rate
2 limiting barrier adjacent the matrix coating.

1 76. A method as in claim 67, wherein the matrix degrades by surface
2 degradation.

1 77. A method as in claim 67, wherein the matrix degrades by bulk
2 degradation.

1 78. A method for luminal substance delivery, said method comprising:
2 providing a luminal prosthesis incorporating and/or coupled to the substance,
3 wherein the prosthesis contains a rate limiting barrier; and
4 implanting the prosthesis in a body lumen so that substantial substance release
5 from the barrier begins after a preselected time period.

1 79. A method as in claim 78, wherein the barrier has a sufficient thickness
2 to allow diffusion of the substance through the barrier.

1 80. A method for luminal substance delivery, said method comprising:
2 providing a luminal prosthesis incorporating or coupled to the substance,
3 wherein the prosthesis contains a nondegradable matrix; and
4 implanting the prosthesis in a body lumen so that substantial substance release
5 from the nondegradable matrix begins after a preselected time period.

1 81. A method as in claim 80, wherein the nondegradable matrix has a
2 sufficient thickness to allow diffusion of the substance through the nondegradable matrix.

1 82. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 4 hours to 24 weeks in a vascular environment.

1 83. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 1 day to 12 weeks in a vascular environment.

1 84. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 2 days to 8 weeks in a vascular environment.

1 85. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 3 days to 50 days in a vascular environment.

1 86. A method for luminal substance delivery, said method comprising:
2 implanting a luminal prosthesis in a lumen of a patient, wherein the prosthesis
3 incorporates and/or couples a substance to be released into the lumen or a luminal wall; and
4 directing energy at the prosthesis to effect release of the substance from the
5 prosthesis.

1 87. A method as in claim 86, wherein the prosthesis incorporates the
2 substance by coating, spraying, dipping, deposition, or painting the substance on the
3 prosthesis.

1 88. A method as in claim 86, wherein the substance is incorporated in a
2 reservoir in or on a scaffold containing the substance.

1 89. A method as in claim 86, wherein the substance is incorporated in a
2 matrix and the matrix coats a scaffold.

1 90. A method as in claim 86, wherein the energy is at least one of
2 ultrasound, magnetic resonance imaging, magnetic field, radio frequency, temperature
3 change, electromagnetic, x-ray, radiation, heat, gamma, or microwave.

1 91. A method for releasing a substance from an implanted device, said
2 method comprising:
3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to the substance; and
5 directing a magnetic field at the device to effect release of the substance from
6 the device.

1 92. A method for releasing a substance from an implanted device, said
2 method comprising:
3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to a matrix formed over the device; and
5 directing a magnetic field at the device to effect release of the particles from
6 the device.

1 93. A method for releasing a substance from an implanted device, said
2 method comprising:
3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to a rate limiting barrier formed over the device; and
5 directing a magnetic field at the device to effect release of the particles from
6 the device.

1 94. A kit comprising:
2 a luminal prosthesis; and
3 instructions on how to implant the prosthesis for luminal substance delivery
4 according to any one of claims 64-93.

1 95. A luminal prosthesis comprising:
2 a scaffold which is implantable within a body lumen; and
3 means on the scaffold for releasing two substances, wherein the two
4 substances are released over two predetermined time patterns comprising an initial phase

5 wherein a substance delivery rate is below a threshold level and a subsequent phase wherein
6 the substance delivery rate is above a threshold level.

1 96. A prosthesis as in claim 95, wherein the means for releasing the two
2 substances comprises a matrix having multiple layers formed over at least a portion of the
3 scaffold.

1 97. A prosthesis as in claim 95, wherein the means for releasing the two
2 substances comprises a rate limiting barrier having multiple layers formed over at least a
3 portion of the scaffold.

1 98. A prosthesis as in claim 95, wherein the two substances are released at
2 different time patterns.

1 99. A prosthesis as in claim 95, wherein a second substance is released
2 after a threshold level of a first substance is reached.

1 100. A prosthesis as in claim 95, wherein the two substances are released
2 simultaneously.

1 101. A prosthesis as in claim 95, wherein the two substances are
2 sequentially released.